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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,909	LOHRAY ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

The Examiner thanks the Applicants for their timely reply filed on 26 March 2008, in the matter of 10/518,909. A response to the remarks and amendments are herein presented under 37 CFR § 1.113.

The Examiner acknowledges that no new claims have been added and that no new matter has been added as a result of amendments made to the claims. It is further noted by the Examiner that the scope of the instant claims have been amended in terms of the claim dependencies. Otherwise stated, all dependent claims have been amended to depend from claim 1.

Claims 1-22 still represent all claims currently presented for examination on the merits.

Response to Remarks

The Abstract and the Title of the Invention have both been amended and thus the objections are **withdrawn**.

The objections to claims 1, 5-7, 15, 17, 19 and 20 are **withdrawn** in view of the amendments made to Applicants' claims.

The rejections made to claims 5 and 14 under *35 USC §112, second paragraph,* are rendered moot in view of Applicants' amendments. Thus the rejections are **withdrawn**.

The rejections made to claim 16 under both *35 USC §112, second paragraph,* and *35 USC §101* are rendered moot in view of Applicants' amendment. The rejection is thus **withdrawn**.

The rejection made to claims 1, 2 and 4-22 under *35 USC §102(b)*, as being anticipated by Bar-Shalom et al. (USPN 5,213,808), is **withdrawn**.

The rejection made to claims 1-15 and 17-22 under *35 USC §103(a)*, as being unpatentable over Bar-Shalom et al. (USPN 5,213,808), is **maintained**.

Information Disclosure Statement

No new Information Disclosure Statements (IDS) have been submitted for consideration.

MAINTAINED REJECTIONS

The following rejection is maintained from the previous Office Action dated 26 October 2007:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15 and 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bar-Shalom et al. (U.S. Patent 5,213,808).

Bar-Shalom et al. teaches a multi-layered article for controlled, pulsatile delivery of an active substance, as described above. Despite teaching the use of both ethyl cellulose and hydrogenated oils as miscible excipients within the same embodiment, Bar-Shalom teaches no specific ratio (e.g. 95:5 to 30:70) of the former to the other the latter.

However, the adjustment of particular conventional working conditions (e.g. determining result effective amounts of the ingredients beneficially taught by the cited references, especially within the broad ranges instantly claimed), is deemed merely a matter of judicious selection and routine optimization, which is well within the purview of the skilled artisan.

Accordingly, this type of modification would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Response to Arguments

Applicants' arguments with regard to the 103(a) over rejection to claims 1-15 and 17-22 have been fully considered, but they are not persuasive.

Applicants argue that the controlled release article practiced by Bar-Shalom ('808 patent) differs from the instantly claimed delivery system on the grounds that the two compositions operate under different delivery mechanisms, that the specific ratio of ethylcellulose to hydrogenated oils is neither taught nor suggested in the '808 patent, and that the particular components/excipients have different uses/roles with regard to the instantly claimed composition versus that which is taught in the art. Applicants further state that the Examiner employs impermissible hindsight in order to establish a case of *prima facie* obviousness.

In response to Applicants' argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure,

such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to Applicants' argument that the references fail to show certain features of Applicants' invention, it is noted that the features upon which Applicants rely (i.e., purpose for using the instantly claimed excipients and the roles of the excipients in the overall delivery system) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regarding Applicants' argument that the mechanisms of operation for both the instantly claimed composition and the article practiced by Bar-Shalom are "entirely different", the Examiner respectfully submits that although claims are read in light of the specification, in order to be given patentable weight, a functional recitation in the claims must be supported by recitation in the claims of sufficient structure to warrant the presence of the functional language. *In re Fuller, 1929 C.D. 172; 388 O.G. 279.* In the instant case, the skilled artisan would not know the particular structure that allows the dosage form to float on the surface of the gastric fluid for a prolonged period from 30 minutes to 10 hours.

Lastly, regarding Applicants' traversal of the compositional ratios taught by the references, the Examiner respectfully submits that Applicants have provided no evidence to conclusively show that optimization of the any of the components, particularly the ratio of ethylcellulose to hydrogenated oils, in accordance with the teachings of Bar-Shalom et al. would lead to a product that is not of the instant claims. Though the specific ratio range is not expressly taught in the '808 patent, optimization of the layer (e.g. coating layer) comprising multiple excipients such as

ethylcellulose and hydrogenated vegetable oils would have been customary and well within the purview of the skilled artisan (col. 15, line 44 to col. 16, line 53). The artisan of ordinary skill would have been highly expected to succeed in achieving the claimed excipient ratios particularly where a motivation the release properties of a coating layer or dosage existed.

As no evidence of criticality has been presented by Applicants on behalf of the aforementioned, the teachings of the reference, as cited in the maintained *35 USC §103* rejection above, continues to read on and render obvious claims 1-15 and 17-22 of the instant application as well as the newly added claim 16, as discussed below.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 5, and 7-10 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the claims recites the limitation "said pharmaceutical aids" in lines 1-2 of each of the claims. There are insufficient antecedent bases for this limitation in the claims. The lack of antecedent basis for the limitation renders the claims indefinite because it is unclear which "pharmaceutical aids" as recited in the dependent claims are used in which of the two layers of the bilayer dosage form, particularly since the use of "pharmaceutical aids" in each of the layers is optional. Herein, and for the purposes of examination on the merits, the Examiner broadly and reasonably interprets the composition of claim 1 as opting to ***not*** include "other pharmaceutical

aids" in either of the claimed layers. As such, dependent claims 4, 5, and 7-10 are further broadly and reasonably interpreted by the Examiner as reciting the same subject matter as the instant claim 1.

Regarding claim 11, the phrase "suitable" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Herein, and for the purposes of examination on the merits, the Examiner broadly and reasonably interprets the phrase "suitable processable form" as a limitation to the therapeutic active agent which allows it to be processed into a dosage form (e.g. dispersed within a polymer matrix).

Regarding claim 15, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-17 and 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Conte et al. (USPN 5,464,633).

The instant claims are directed to a bilayer pharmaceutical dosage form comprising: (1) a first layer which itself comprises a mixture of low bulk density pharmaceutical excipients

consisting of polymers such as ethylcellulose and additional compounds such as hydrogenated oils, waxes or fatty acids; and (2) a second layer which itself comprises the therapeutically active agent and controlled-release matrix polymers (claims 1, 4, 5, 7-10, 12, 14, 17, 19 and 22). Claims 4, 5 and 7-10, recite the same subject matter as claim 1, as discussed above. Wherein the therapeutically active agent has a "narrow absorption window in the gastrointestinal tract" as recited in the instant claim 12, is considered by the Examiner to be an inseparable property of the drug (see MPEP §2112.02(II)). The limitation recited in claim 14 wherein the drug is "for local treatment of the gastrointestinal tract", is considered by the Examiner as a recitation of intended use and thus holds no patentable merit since said use does not impact the instantly claimed composition (see MPEP §2111). The limitation recited in claim 17 wherein the two layers of the composition are prepared by granulation or compression, is considered by the Examiner to be a product-by-process limitation, which also holds no patentable weight with regard to the composition it purports to create (see MPEP §2113). With regard to the functional limitation recited in claim 19 "wherein the dosage form floats on the surface of the gastric fluid for [a] prolonged period from 0.5 to 10 hours", until some material difference(s) in the properties of the composition are demonstrated, said limitation is considered by the Examiner to be directed toward the instantly claimed bilayer composition. Claim 22 is viewed by the Examiner as reading on the subject matter of claim particularly since it recites a product-by-process limitation (e.g. "prepared according to the present invention") as well as an intended use (e.g. "suitable for human administration"). The combination of ethylcellulose and hydrogenated oils in the first layer is recited in claim 2. Controlled-release matrix polymers for the second layer are recited in claim 6. Limitations to the therapeutically active agent are recited (claims 11, 13 and 15). Claim 20 recites

the bilayer dosage form of claim 1 as being coated with either a rapidly dissolving water soluble film-forming polymer or a rapidly dissolving pharmaceutical excipient. With regard to the former, the Examiner interprets this limitation in light of Applicants' specification as including cellulose derivatives such as hydroxypropyl methylcellulose and ethylcellulose (see pg. 11, lines 23-24). Forms of the bilayer composition are recited in claim 21. A method of using the composition of claim 1 comprising oral administration to a human patient is recited in claim 16.

Conte teaches gastroresistant and enterosoluble bilayer tablets having a core which comprises a therapeutically active agent and an aqueously-responsive polymeric substance, a layer applied externally to said core and a coating (Abstract and Figure 1). The pharmaceutical bilayer tablet for oral administration is taught as having a core layer and an external layer which is applied to the core via compression (claim 1). Said core layer is further taught as comprising an active substance and a controlled release polymeric matrix comprised of hydroxypropyl methylcellulose (HPMC), whereas said external layer is taught as comprising compounds such as adjuvants and excipients (claim 1). Ethylcellulose and hydrogenated castor oil are taught as specific adjuvant and excipient substances which are used in the external layer (claim 14). The active agent is taught as being dispersed in a tablet core comprising HPMC (claim 1 and Example 1). General categories of therapeutic active agents such as non-steroidal anti-inflammatory drugs (NSAIDs) as well as specific active agents such as diltiazem are taught (claims 2 and 4, respectively). Figure 1 and claim 15 teach the presence of a coating which surrounds the bilayer tablet and consists cellulose derived polymeric materials such as cellulose acetophthalate, cellulose acetopropionate or cellulose trimellitate.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conte et al. (USPN 5,464,633).

The instant claims are directed to a bilayer pharmaceutical dosage form, as discussed above. Claims 3 and 18 respectively recite a ratio of ethylcellulose to hydrogenated oils and a mass range for the presence of the active agent in the core.

The teachings to Conte et al. are discussed above.

However, Conte does not expressly teach either the ratio of ethylcellulose to hydrogenated oils or the range of active agent present, as claimed by Applicants. Since the values and formats of each parameter with respect to the claimed composition are adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary

skill in the art to employ. For example, Conte teaches at claim 6 that the core of the tablet contains a percentage of polymeric substance ranging from 1-90% by weight of the core, thereby demonstrating that the active substance is similarly adjustable. Examples 1b and 4b also teach different granular formulations used as external layers for the tablet cores. Thus, it would have been customary for an artisan of ordinary skill, to adjust the ratio of the claimed ratio of ethylcellulose to hydrogenated oils in the composition, particularly in view of the Examples and claim 14, in order to achieve the desired controlled-release, coated, bilayer tablet. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

All claims have been rejected; no claims are allowed.

Conclusion

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615